

SEQUENCE LISTING <110> VUILLARD, LAURENT MICHEL MARIE PATEL, SAHIL JOE YON, JEFFREY ROLAND CLEASBY, ANNE HAMILTON, BRUCE JOHN SHAH, ALEEM <120> CRYSTAL STRUCTURE OF BETA SITE APP CLEAVING ENZYME (BACE) AND METHODS OF USE THEREOF <130> 674553-2002.1 <140> 10/627,473 <141> 2003-07-25 <150> 60/398,681 <151> 2002-07-26 <160> 46 <170> PatentIn Ver. 2.1 <210> 1 <211> 1368 <212> DNA

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Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala 145 150 155 160

Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser 165 170 175

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Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu 210 215 220

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Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr 85 90 95

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Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val Thr Val Arg Ala 145 150 155 160

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Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly 130 135 140

Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala 145 150 155 160

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- Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile
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- Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn 260 265 270
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- Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys 370 375 380
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- Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met
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- Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly 85 90 95
- Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg
- Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly
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- Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr 130 135 140
- Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn 145 150 155 160
- Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn 165 170 175
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- Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val 195 200 205
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- Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly 260 265 270
- Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile 275 280 285
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<211> 461

<212> PRT

<213> Homo sapiens

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Gly Val Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu 20 25 30

Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu 35 40 45

Thr Asp Glu Glu Pro Glu Pro Gly Lys Lys Gly Ser Phe Val Glu 50 55 60

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu 65 70 ' 75 80

Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr 85 90 95

Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His 100 105 110

Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys
115 120 125

Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly 130 135 140

Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val Thr Val Arg Ala 145 150 155 160

Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Gln Gly Ser 165 170 175

Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro 180 185 190

Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His 195 200 205

Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu 210 215 220

Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly 225 230 235 240

Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile 245 250 255

Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn 260 265 270

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Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser
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Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe
Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe
305
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                                         315
Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly
Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly
Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr
Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys
                        375
Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile
                    390
Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly
Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala
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Ile Pro Gln Thr Asp Glu Ser His His His His His
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ggtatcgacc actcgctgta cacaggcagt ctctggtata cacccatccg gcgggagtgg 780
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<210> 14

<211> 455

<212> PRT

<213> Homo sapiens

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Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu 35 40 45

Thr Asp Glu Glu Pro Glu Glu Pro Gly Lys Lys Gly Ser Phe Val Glu 50 55 60

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu 65 70 75 80

Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr 85 90 95

Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His 100 105 110

Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys 115 120 125

Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly 130 135 140

Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val Thr Val Arg Ala 145 150 155 160

Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Gln Gly Ser 165 170 175

Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro 180 185 190

Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His 195 200 205 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu 210 215 220

Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly 225 230 235 240

Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile 245 250 255

Arg Arg Glu Trp Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn 260 265 270

Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser 275 280 285

Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe 290 295 300

Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe 305 310 315 320

Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly 325 330 335

Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly 340 345 350

Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr 355 360 365

Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys 370 375 380

Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile 385 390 395 400

Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly 405 410 415

Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala 420 425 430

Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn 435 440 445

Ile Pro Gln Thr Asp Glu Ser 450 455

<210> 15

<211> 1386

<212> DNA

<213> Homo sapiens

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ggettecece tecageagte tgaagtgetg geetetgteg gagggageat gateattgga 720
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135

<210> 16

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- Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Gln Gly Ser 165 170 175
- Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro 180 185 190
- Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His 195 200 205
- Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu 210 215 220
- Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly 225 230 235
- Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile 245 250 250
- Arg Arg Glu Trp Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn 260 265 270
- Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser 275 280 285
- Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe 290 295 300
- Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe 305 310 315 320
- Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly 325 330 335
- Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly 340 345 350
- Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr 355 360 365
- Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys 370 375 380
- Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile 385 390 395 400
- Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly 405 410 415
- Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala 420 425 430
- Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn 435 440 445

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<211> 1383
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<213> Homo sapiens
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<210> 18
<211> 460
<212> PRT
<213> Homo sapiens
<400> 18
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Gly Val Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu
Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu
Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Gly Ser Phe Val Glu Met
Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met
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- Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly
  85 90 95
- Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg 100 105 110
- Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly
  115 120 125
- Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr 130 135 140
- Asp Leu Val Ser Ile Pro His Gly Pro Gln Val Thr Val Arg Ala Asn 145 150 155 160
- Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Gln Gly Ser Asn 165 170 175
- Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp 180 185 190
- Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val 195 200 205
- Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Gln 210 215 220
- Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly 225 230 235 240
- Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg
  245 250 255
- Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly
  260 265 270
- Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile 275 280 285
- Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu 290 295 300
- Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro 305 310 315 320
- Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr
- Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu 340 345 350
- Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu 355 360 365
- Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe 370 375 380

Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met 385 390 395 400

Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe
405 410 415

Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val 420 425 430

Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile 435 440 445

Pro Gln Thr Asp Glu Ser His His His His His 450 455 460

<210> 19

<211> 411

<212> PRT

<213> Homo sapiens

<400> 19

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Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly 20 25 30

Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile 35 40 45

Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His 50 55 60

Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg 65 70 75 80

Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu 85 90 95

Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val 100 105 110

Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe 115 120 125

Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu 130 135 140

Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val 145 150 155 160

Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala 165 170 175

Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser 180 185 190 Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp 195 200 205

Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg 210 215 220

Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn 225 230 235 240

Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro 245 250 255

Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser 260 265 270

Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys 275 280 285

Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu 290 295 300

Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu 305 310 315 320

Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp 325, 330 335

Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met 340 345 350

Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg 355 360 365

Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe 370 375 380

Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp 385 390 395 400

Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser 405 410

<210> 20

<211> 411

<212> PRT

<213> Homo sapiens

<400> 20

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Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly
20 25 30

Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile 35 40 45

Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His 50 55 60

Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg 65 70 75 80

Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu 85 90 95

Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val 100 105 110

Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe 115 120 125

Ile Gln Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu 130 135 140

Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val 145 150 155 160

Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala 165 170 175

Gly Phe Pro Leu Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser 180 185 190

Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp 195 200 205

Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg 210 215 220

Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn 225 230 235 240

Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro 245 250 255

Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser 260 265 270

Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys 275 280 285

Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu 290 295 300

Tyr Leu Met Gly Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu 305 310 315 320

Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp 325 330 335

Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met 340 345 350

Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg 355 360 365

Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe 370 375 380

Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp 385 390 395 400

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<210> 21

<211> 417

<212> PRT

<213> Homo sapiens

<400> 21

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Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile 35 40 45

Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His 50 55 60

Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg 65 70 75 80

Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu 85 90 95

Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Gln Val

Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe 115 120 125

Ile Gln Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu 130 135 140

Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val 145 150 155 160

Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala 165 170 175

Gly Phe Pro Leu Gln Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser 180 185 190 Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp 195 200 205

Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg 210 215 220

Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn 225 230 235 240

Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro 245 250 255

Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser 260 265 270

Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys 275 280 285

Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu 290 295 300

Tyr Leu Met Gly Glu Val Thr Gln Gln Ser Phe Arg Ile Thr Ile Leu 305 310 315 320

Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp 325 330 335

Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met 340 345 350

Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg 355 360 365

Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe 370 380

Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp 385 390 395 400

Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser His His His His 405 410 415

His

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<211> 24

<212> DNA

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<220>

<223> Description of Artificial Sequence: Primer

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ccacaggtgc catctgtgtc tcc
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<211> 22
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                                                                    22
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catctccaca aagctgccct tcttgccggg ctcctcggg
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                                                                    42
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<211> 39
<212> DNA
<213> Homo sapiens
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                                                                    39
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<212> DNA
<213> Homo sapiens
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<400> 38				•
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<212> DNA
<213> Homo sapiens
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<211> 6
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: 6-His tag
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His His His His His
<210> 43
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<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: Primer
<400> 43
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<210> 44
<211> 40
<212> DNA
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<211> 18
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     oligonucleotide sequence
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18

<210> 46 <211> 12 <212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence: Illustrative synthetic flourescent peptide

Arg Glu Glu Val Asn Leu Asp Ala Glu Phe Lys Arg 5